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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,700	04/07/2006	Johannes Bonenberger	DEBE:056US/10502411	2064

32425 7590 03/05/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
03/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,700	BONENBERGER ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-11 and 13-17* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-11 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 16, 2008 has been entered.

Status of the Claims

2. This action is in response to papers filed on December 16, 2008.

3. Claims 1, 3, 8 and 15 were amended. Claims 5 and 12 were cancelled.

4. The previous rejections under 35 USC § 102 (b) and 103 (a) not reiterated below have been withdrawn. Applicant's arguments filed December 16, 2008 have been thoroughly reviewed and are addressed following the rejections.

5. Claim 11 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention of group II there being no allowable generic or linking claim in the reply filed on July 5, 2007.

6. Proper status identifier for the withdrawn claim 11 have been reviewed and entered.

7. Claims 1-4, 6-11 and 13-17 are pending in this application and claims 1-4, 6-10 and 13-17 are under examination.

Priority

8. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. In view of the claimed priority to application 10245644.5 filed in Germany, the effective filing date for the instant application is September 30, 2002.

Amendments to Claims

9. Amendments to the claims 1, 3, 8 and 15 have been reviewed and entered.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-2 and 6-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Collier et al (USPN 5,985,548 filed Apr. 22, 1998).

Regarding claim 1, Collier et al teaches a competitive binding assay for detecting analytes comprising following steps.

Regarding step 'a', Collier et al teaches incubating a sample with a ligand reporter conjugates (Fig. 6, analyte – labeled as A, ligand reporter conjugate –labeled as Q, column 9, lines 60-67) and further teaches that ligand comprises an analyte

antibody and the reporter is a nucleic acid (column 4, lines 53-59, column 7, lines 10-25). The nucleic acids of Collier et al are the macromolecules as claimed. Collier et al also teaches that at least two molecules of the ligand, i.e., analyte to be detected are coupled (column 17, lines 6-35).

Regarding step 'b', Collier et al teaches incubating the sample with solid carrier to which capture molecules for the analyte to be detected are coupled (Fig. 6, solid carrier with capture molecules – labeled as B, column 9, lines 63-65).

Regarding step 'c', Collier et al teaches adding ethidium bromide dye (i.e., fluorescence dye) to stain nucleic acids, i.e., macromolecules (column 22, lines 49-52 and 64-67).

Regarding step 'd', Collier et al teaches that the ligand reporter conjugate competes with the analyte for binding sites on the capture molecules immobilized on the solid carrier (Fig. 6, See STEP b, column 10, lines 1-25), Collier et al further teaches that in the presence of analyte, the analyte binds to the solid carrier (Fig. 6, STEP b, right side, column 10, lines 1-4) and the ligand reporter conjugates remains unbound to the solid carrier (Fig. 6, STEP b, left side, column 10, lines 1-4). Collier et al also teaches that in case wherein analyte is bound to capture molecules on the solid carrier, no nucleic acid replication occurs and nucleic acids are not detected (column 10, lines 11-18). Collier also teaches that the detection of analyte via nucleic acids, i.e., macromolecules bound to the solid carrier using a variety of techniques, one of which is by excitation of the ethidium bromide fluorescence dye (column 10, lines 1-25, column 22, lines 49-67). Combined teachings of Collier et al encompass, wherein in the

presence of analyte in the sample will reduce the signal produced by binding of the ligand reporter conjugate (i.e., macromolecule- bound analyte) to the capture molecule coupled to the solid carrier as claimed.

Regarding claim 2, Collier et al teaches removing non-bound fluorescence dye from the solid carrier by size separation (column 22, lines 55-57), which meets the limitation of after step 'c' a further step 'c')' of removing the non-bound fluorescence dye from solid carrier.

Regarding claim 6, Collier et al teaches that the nucleic acids, i.e., macromolecules are single strand oligonucleotides of length in the range of 20 to 5000 bases (column 12, lines 48-49 and 54-55), which encompasses the range from 40 to 80 nucleotides as claimed.

Regarding claim 7, Collier et al teaches that the reporter nucleic acids (i.e., macromolecules) detect the same analyte (Fig. 6 and column 10, lines 11-18), thus teaching macromolecules are identical.

Regarding claim 8, Collier et al teaches that the ligand is one member of the analyte and further teaches (column 7, lines 10-11) and further teaches that ligand has molecular weight of less than 3000 Dalton (column 17, lines 16-19), which is less than 5000 Dalton as claimed.

Regarding claim 9, Collier et al teaches that the fluorescence dye is a fluorophore (column 22, lines 65-67).

Regarding claim 10, Collier et al teaches that the solid carrier polypropylene or glass (column 10, lines 5767), which is permeable to light and the detection method is implemented by means of a transmitted-light method (column 40, lines 59-61).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3-4, and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collier et al (USPN 5,985,548 filed Apr. 22, 1998) in view of Reddy et al (USPN 5,648,213 issued Jul. 15, 1997).

Regarding claim 3, Collier et al teaches a competitive binding assay for detecting analytes comprising following steps.

Regarding step 'a', Collier et al teaches incubating a sample with a ligand reporter conjugates (Fig. 6, analyte – labeled as A, ligand reporter conjugate –labeled as Q, column 9, lines 60-67) and further teaches that ligand comprises an analyte antibody and the reporter is a nucleic acid (column 4, lines 53-59, column 7, lines 10-25). The nucleic acids of Collier et al are the macromolecules as claimed. Collier et al also teaches that at least two molecules of the ligand, i.e., analyte to be detected are coupled (column 17, lines 6-35). Collier et al are silent about fluorescence dye marked nucleic acid molecule, i.e., macromolecule.

Regarding step 'b', Collier et al teaches incubating the sample with solid carrier to which capture molecules for the analyte to be detected are coupled (Fig. 6, solid carrier with capture molecules – labeled as B, column 9, lines 63-65).

Regarding step 'c', Collier et al teaches that the ligand reporter conjugate competes with the analyte for binding sites on the capture molecules immobilized on the solid carrier (Fig. 6, See STEP b, column 10, lines 1-25), Collier et al further teaches that in the presence of analyte, the analyte binds to the solid carrier (Fig. 6, STEP b, right side, column 10, lines 1-4) and the ligand reporter conjugates remains unbound to the solid carrier (Fig. 6, STEP b, left side, column 10, lines 1-4). Collier et al also teaches that in case wherein analyte is bound to capture molecules on the solid carrier, no nucleic acid replication occurs and nucleic acids are not detected (column 10, lines 11-18). Collier also teaches that the detection of analyte via nucleic acids, i.e., macromolecules bound to the solid carrier using a variety of techniques, one of which is by excitation of the ethidium bromide fluorescence dye (column 10, lines 1-25, column

22, lines 49-67). Combined teachings of Collier et al encompass, wherein in the presence of analyte in the sample will reduce the signal produced by binding of the ligand reporter conjugate (i.e., macromolecule- bound analyte) to the capture molecule coupled to the solid carrier as claimed.

Regarding claim 4, Collier et al teaches that the unbound ligand reporter conjugates are removed by washing (column 10, lines 1-6).

Regarding claim 13, Collier et al teaches that the nucleic acids, i.e., macromolecules are single strand oligonucleotides of length in the range of 20 to 5000 bases (column 12, lines 48-49 and 54-55), which encompasses the range from 40 to 80 nucleotides as claimed.

Regarding claim 14, Collier et al teaches that the reporter nucleic acids (i.e., macromolecules) detect the same analyte (Fig. 6 and column 10, lines 11-18), thus teaching macromolecules are identical.

Regarding claim 15, Collier et al teaches that the ligand is one member of the analyte and further teaches (column 7, lines 10-11) and further teaches that ligand has molecular weight of less than 3000 Dalton (column 17, lines 16-19), which is less than 5000 Dalton as claimed.

Regarding claim 16, Collier et al teaches that the fluorescence dye is a fluorophore (column 22, lines 65-67).

Regarding claim 17, Collier et al teaches that the solid carrier polypropylene or glass (column 10, lines 57-67), which is permeable to light and the detection method is implemented by means of a transmitted-light method (column 40, lines 59-61).

As described above, Collier et al are silent about marking nucleic acid, i.e., a macromolecule with a fluorescence dye. However marking nucleic acid, i.e., a macromolecule with a fluorescence dye was known in the art at the time of the claimed invention was made as taught by Reddy et al.

Reddy et al teaches a competitive assay comprising the steps of incubating a sample comprising analytes with oligonucleotide bound analyte (column 3, lines 53-67), thus teaching to each oligonucleotide at least one molecule of the analyte to be detected in the sample are coupled and the macromolecule consists of nucleic acids as claimed. Reddy et al also teaches that the oligonucleotide bound analyte competes with the target analyte for the immunoreactant comprising a fluorescein label (column 3, lines 53-64), thus teaching when oligonucleotide bound analyte binds to the immunoreactant, the nucleic acid, i.e., macromolecule is marked with fluorescent dye. Reddy et al further teaches that the analyte comprises phenobarbital, theophylline, hormones and smaller analytes (column 3, lines 43-46, column 15, lines 57-58). Reddy et al also teaches that competition assay comprising fluorescence dye marked nucleic acid (i.e., macromolecule) is particularly useful for detecting the presence of smaller and multiple analytes in the sample (column 3, lines 40-46).

Collier et al explicitly teaches that the competitive binding assays can be practiced employing alternative protocols (column 10, lines 19-24). Adopting the competitive binding assay format of Reddy et al in the method of Collier et al provides a means for detecting multiple and smaller sized analytes in the method of Collier et al.

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the macromolecule in the method of Collier et al with fluorescence dye marked macromolecules of Reddy et al with a reasonable expectation of success.

The artisan would have been motivated to modify the macromolecule in the method of Collier et al with the expected benefit of detecting the presence of smaller and multiple analytes in the sample as taught by Reddy et al (column 3, lines 40-46).

12. Claims 1-4, 6-10 and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al (USPN 5,648,213 issued Jul. 15, 1997) in view of Collier et al (USPN 5,985,548 filed Apr. 22, 1998).

Regarding claim 1, Reddy et al teaches a competitive binding assay for detecting analytes comprising following steps.

Regarding step 'a', Reddy et al teaches incubating a sample comprising analytes with oligonucleotide bound analyte (column 3, lines 53-67), thus teaching to each oligonucleotide at least one molecule of the analyte to be detected in the sample are coupled and the macromolecule consists of nucleic acids as claimed. Reddy et al also teaches that the analyte is phenobarbital, theophylline, hormones, drugs and smaller sized analytes (column 3, lines 43-46, column 15, lines 57-58). Reddy et al are silent about at least two molecules of the analyte to be detected are coupled to oligonucleotides.

Regarding step 'b', Reddy et al teaches further incubating the sample with solid carrier to which complementary oligonucleotides, i.e., capture molecules for the analyte to be detected are coupled (column 3, lines 56-58 and column 4, lines 1-3).

Regarding step 'c', Reddy et al teaches adding immunoreactant labeled with fluorescein dye to stain nucleic acids, i.e., macromolecules (column 3, lines 61-65).

Regarding step 'd', Reddy et al teaches detecting the analyte present in the sample by excitation of the fluorescent dye (column 4, lines 5-10 and column 9, lines 61-64), wherein in the presence of analyte in the sample will reduce the signal produced by binding of the oligonucleotide analyte conjugate (i.e., macromolecule- bound analyte) to the capture molecule coupled to the solid carrier as claimed (column 4, lines 3-6).

Regarding claim 3, Reddy et al teaches a competitive binding assay for detecting analytes comprising following steps.

Regarding step 'a', Reddy et al teaches incubating a sample comprising analytes with oligonucleotide bound analyte and an immunoreactant (column 3, lines 53-67), which meets the limitation of to each oligonucleotide at least one molecule of the analyte to be detected in the sample are coupled and the macromolecule consists of nucleic acids as claimed. Reddy et al also teaches that the oligonucleotide bound analyte competes with the target analyte for the immunoreactant comprising a fluorescein label (column 3, lines 53-64), thus teaching when oligonucleotide bound analyte binds to the immunoreactant, the nucleic acid, i.e., macromolecule is marked with fluorescent dye. Combined teachings of Reddy et al encompass incubating sample with fluorescence dye marked macromolecules as claimed.

Reddy et al also teaches that the analyte is phenobarbital, theophylline, hormones, drugs and smaller sized analytes (column 3, lines 43-46, column 15, lines 57-58). Reddy et al are silent about at least two molecules of the analyte to be detected are coupled to oligonucleotides.

Regarding step 'b', Reddy et al teaches further incubating the sample with solid carrier to which complementary oligonucleotides, i.e., capture molecules for the analyte to be detected are coupled (column 3, lines 56-58 and column 4, lines 1-3).

Regarding step 'c', Reddy et al teaches detecting the analyte present in the sample by excitation of the fluorescent dye (column 4, lines 5-10 and column 9, lines 61-64), wherein in the presence of analyte in the sample will reduce the signal produced by binding of the oligonucleotide analyte conjugate (i.e., macromolecule- bound analyte) to the capture molecule coupled to the solid carrier as claimed (column 4, lines 3-6).

Regarding claim 2, Reddy et al teaches removing non-bound fluorescence dye from the solid carrier before detection by washing (column 4, lines 8-10), which meets the limitation of after step 'c' a further step 'c')' of removing the non-bound fluorescence dye from solid carrier.

Regarding claim 4, Reddy et al teaches a wash step for removing residual solution comprising non-bound macromolecules (column 4, lines 8-10), which meets the limitation of after step 'a' a further step 'a')' of removing the non-bound macromolecules.

Regarding claims 6 and 13, Reddy et al teaches that the nucleic acids, i.e., macromolecules are single strand oligonucleotides of length in the range of 6 to 30 bases (column 5, lines 30-35) but are silent about the range from 40 to 80 nucleotides.

Regarding claims 7 and 14, Reddy et al teaches that the oligonucleotides are (i.e., macromolecules) detect the same analyte or different analytes (column 3, lines 40-67), thus teaching macromolecules are identical or non identical.

Regarding claims 8 and 15, Reddy et al teaches the analyte is theophylline or Phenobarbital (column 15, lines 57-58), which has a molecular weight less than 5000 Dalton.

Regarding claims 9 and 16, Reddy et al teaches that the fluorescence dye is a fluorescein, i.e., a fluorophore (column 3, lines 62-64).

Regarding claims 10 and 17, Reddy et al teaches that the solid carrier is transparent (column 9, lines 32-37), which is permeable to light and the detection method is implemented by means of a transmitted-light method (column 9, lines 44-56).

As described above, regarding claims 1 and 3, Reddy et al are silent about at least two molecules of the analyte to be detected are coupled to oligonucleotides, i.e., macromolecules.

Regarding claims 6 and 13, Reddy et al are silent about the range from 40 to 80 nucleotides.

However, at least two molecules of the analyte to be detected are coupled to oligonucleotides, i.e., macromolecules and the oligonucleotides lengths were known in the art at the time of the claimed invention was made as taught by Collier et al.

Collier et al teaches a competitive binding assay for detecting analytes comprising incubating a sample with a ligand reporter conjugates (Fig. 6, analyte – labeled as A, ligand reporter conjugate –labeled as Q, column 9, lines 60-67) and

further teaches that ligand comprises an analyte antibody and the reporter is a nucleic acid (column 4, lines 53-59, column 7, lines 10-25). The nucleic acids of Collier et al are the macromolecules as claimed. Collier et al also teaches that at least two molecules of the ligand, i.e., analyte to be detected are coupled (column 17, lines 6-35).

Regarding claims 6 and 13, Collier et al teaches that the nucleic acids, i.e., macromolecules are single strand oligonucleotides of length in the range of 20 to 5000 bases (column 12, lines 48-49 and 54-55), which encompasses the range from 40 to 80 nucleotides as claimed.

Collier et al also teaches adding two molecules of the analyte to be detected to the macromolecules achieve maximum sensitivity of the assay (column 17, lines 29-35).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the step of coupling analytes to the macromolecule in the method of Reddy et al with macromolecule comprising two molecules of the analytes of Collier et al with a reasonable expectation of success.

The artisan would have been motivated to modify the step of coupling analytes to the macromolecule in the method of Reddy et al with the expected benefit of achieving maximum sensitivity of the assay as taught by Collier et al (column 17, lines 29-35).

Response to remarks from the Applicants

Claim Rejections under 35 U.S.C. § 102(b)

13. Applicant's arguments with respect to claims 1, 3, 7, 9, 10, 14, 16 and 17 being anticipated by Zoha et al have been fully considered (Remarks, section II) but are moot

in view of withdrawal of the previous rejection and the new grounds of rejection as set forth in this office action necessitated by claim amendments.

Claim Rejections under 35 U.S.C. § 103(a)

14. Applicant's arguments filed on December 16, 2008 being unpatentable over Zoha et al in view of Schobell et al, Zoha et al in view of Cross et al, Zoha et al in view of Nilsen et al (Remarks, section III) but are moot in view of withdrawal of the previous rejections and the new grounds of rejection as set forth in this office action necessitated by claim amendments.

Conclusion

15. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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/Narayan K. Bhat/

Examiner, Art Unit 1634

/Ram R. Shukla/

Supervisory Patent Examiner, Art Unit 1634